Multiple Sclerosis and Related Disorders 12 (2017) 15–19

Contents lists available at ScienceDirect

Multiple Sclerosis and Related Disorders

journal homepage: www.elsevier.com/locate/msard

Sensitivity of visual evoked potentials and spectral domain optical coherence tomography in early relapsing remitting multiple sclerosis

Raed Behbehani[a,b,*], Samar Ahmed[c,d], Jasem Al-Hashel[c,e], Rossen T. Rousseff[c], Raed Alroughani[a,f]

[a] Opthalmology Clinic, Dasman Institute, Dasman, Kuwait
[b] Al-Bahar Ophthalmology Center, Ibn Sina Hospital, Kuwait
[c] Department of Neurology, Ibn Sina Hospital, Kuwait
[d] Department of Neurology and Psychiatry, Minia University, Egypt
[e] Department of Medicine, Faculty of Medicine, Kuwait University, Kuwait
[f] Division of Neurology, Amiri Hospital, Sharq, Kuwait

ARTICLE INFO

Keywords:
Optical coherence tomography
Retinal nerve fiber layer
Ganglion cell/inner plexiform layer
Multiple sclerosis
Axonal loss
Visual evoked potentials

ABSTRACT

Background: Visual evoked potentials and spectral-domain optical coherence tomography are common ancillary studies that assess the visual pathways from a functional and structural aspect, respectively.
Objective: To compare prevalence of abnormalities of Visual evoked potentials (VEP) and spectral-domain optical coherence tomography (SDOCT) in patients with relapsing remitting multiple sclerosis (RRMS).
Methods: A cross-sectional study of 100 eyes with disease duration of less than 5 years since the diagnosis. Correlation between retinal nerve fiber layer and ganglion-cell/inner plexiform layer with pattern-reversal visual evoked potentials amplitude and latency and contrast sensitivity was performed.
Results: The prevalence of abnormalities in pattern-reversal visual VEP was 56% while that of SOCT was 48% in all eyes. There was significant negative correlations between the average RNFL ($r=-0.34$, $p=0.001$) and GCIPL ($r=-0.39$, $p < 0.001$) with VEP latency. In eyes with prior optic neuritis, a significant negative correlation was seen between average RNFL ($r=-0.33$, $p=0.037$) and GCIPL ($r=-0.40$, $p=0.010$) with VEP latency.
Conclusions: We have found higher prevalence of VEP abnormalities than SCOCT in early relapsing-remitting multiple sclerosis. This suggests that VEP has a higher sensitivity for detecting lesions of the visual pathway in patients with early RRMS.

1. Introduction

Multiple Sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system characterized by relapses in its early course and subsequent progression over time. The visual pathways are commonly involved in MS as an initial manifestation in the form of optic neuritis, or during the course of the disease (Optic Neuritis Study Group, 2008). Visual pathways lesions can be detected by delayed visual-evoked potentials (VEP) latencies and axonal loss using optical coherence tomography (OCT) even in patients with no clinical visual manifestations (Naismith et al., 2009; Klistorner et al., 2013; Alshowaeir et al., 2014; Sriram et al., 2014). Therefore, detecting sub-clinical lesions of the visual pathway has become a diagnostically significant aspect in the assessment of newly diagnosed MS cases (Galetta and Balcer, 2013). VEP assesses visual pathway functional integrity from the retina to the occipital cortex by measuring the latencies, amplitudes and symmetry of cortical responses to standardized visual stimuli. OCT, given its high spatial resolution however, is useful in assessing structural changes in the retinal layers arising from axonal loss and neurodegeneration (Kolappan et al., 2009). Few studies have compared the prevalence of abnormalities of VEP compared to OCT in MS patients with and without history of optic neuritis (Naismith et al., 2009; Klistorner et al., 2013; Di Maggio et al., 2014; Chilinska et al., 2015). Some of these studies were done using time-domain OCT, which has a lower spatial resolution than the current spectral-domain OCT (SDOCT). Segmentation algorithms in SDOCT measure individual retinal layers including the ganglion-cell/inner plexiform layer (GCIPL), which can serve as an additional structural index for correlation with functional tests such as VEP and contrast sensitivity.

* Correspondence to: FRCSC, P.O Box 1180, Dasman 15462, Kuwait.
E-mail address: raed.behbehani@dasmaninstitute.org (R. Behbehani).

http://dx.doi.org/10.1016/j.msard.2016.12.005
Received 27 April 2016; Received in revised form 26 November 2016; Accepted 10 December 2016

2. Methods

This is a cross-sectional study conducted at the MS clinic in Dasman Institute. Subjects who were at least 18 year old with RRMS according to the revised 2010 McDonald diagnostic criteria, had a disease duration of less than 5 years since the since the diagnosis, and expanded disability status scale (EDSS) scores ≤3.5 were included (Polman et al., 2011). Patients with progressive MS (primary or secondary), disease duration of more than 5 years, other demyelinating disorders (neuromyelitis optica or acute disseminated encephalomyelitis), high refractive error (±6 diopters) or who had optic neuritis onset within the 6 months of assessment, were excluded. All patients had neuro-ophthalmologic assessment and were tested using Pelli-Rosbon contrast sensitivity charts at one meter (Metropia Ltd. Cambridge, UK) and were given a logarithmic score. Patients` demographics (age, gender), clinical characteristics (age at disease onset, disease duration, presentation at onset, baseline EDSS score) were obtained from their medical records. We have performed both VEP and SDOCT on our study subjects within 6-month period of each other. The objective of this study was to compare the prevalence of abnormalities in VEP compared to SDOCT in early RRMS patients with and without optic neuritis. Furthermore, the correlations between VEP p-100 latency and amplitude with peri-papillary retinal nerve fiber layer (RNFL), ganglion-cell/inner plexiform layer (GCIPL), and Pelli-Robson contrast sensitivity logarithmic score were assessed. This study was approved by the ethical committee of Dasman Institute and all patients provided written informed consents.

2.1. OCT

Data of SDOCT results (average and all quadrants RNFL thickness, ganglion cell/inner plexiform layer thickness) were obtained using SDOCT (Cirrhus HDOCT 5000; Carl Zeiss Meditec). The SDOCT scan was performed by an experienced operator and only measurements of good quality and adequate signal strength were included.

OCT was considered abnormal if at least one quadrant of the RNFL and/or the average ganglion cell/inner plexiform layer thickness were 2 standard deviations lower than the built-in normal values of the, $p < 0.05$, in either eye of a single patient.

2.2. VEP

Pattern-reversal VEP was recorded by the same qualified neurophysiology technician on a 4-channel EP machine (Natus Keypoint TM). We followed the standard techniques according to the Guideline of American Clinical Neurophysiology Society (American Clinical Neurophysiology Society, 2006). The P100 latency and the highest peak to peak amplitude in the N75-P100-N145 complex were measured by placing the cursors manually. On the Fz-mastoid channel, the N100 frontal potential was identified and used to identify possible sources of abnormality in the shape of the VEP. The patients were seated 1 m in front of the stimulator in a dark quiet environment. Subjects with refractory anomalies used their appropriate corrective lenses during the recording. They were instructed to focus attentively their vision on the marker in the center of the stimulating screen and to be as relaxed and calm as possible during the study. Evoked responses were recorded from Oz, O1 and O2 electrode sites with the reference over the Fz; and from Fz referred to one of the mastoids (all positions designated according to the International 10–20 system), at impedance below 5 kOhm, filter bandwidth 1–100 Hz, sensitivity 5 microV division and epoch of 300 ms. Pattern-reversal stimuli were delivered by an oscilloscope screen, that represented 12° visual angle in the patients visual fields. White and black checkerboard stimuli with a size of 32′ visual angle and reversal frequency of 3 Hz were delivered. At least 200 traces were recorded by monocular stimulation and averaged from each eye. The P100 latency and the highest peak to peak amplitude in the N75-P100-N145 complex were measured by placing the cursors manually. On the Fz-mastoid channel, the N100 frontal potential was identified and used to identify possible sources of abnormality in the shape of the VEP.

VEP was considered abnormal if any of the following criteria was fulfilled; (1) Absolutely prolonged latency in one or both eyes (P100 more than 108 ms in females and more than 110 ms in males). (2) Side-to-side difference of P-100 latency of more than 7 ms, (3) Absolute decrease of VEP amplitude, (4) Side-to-side amplitude ratio of more than 2:1. Our control values for detecting abnormality are based on our laboratory normal values for adults, derived from a study of 110 healthy controls (age 18–55 years, median 32 years, 64 male) and represent the 97.5th percentile of the obtained data for each parameter.

2.2.1. Statistical analysis

All statistical analyses were performed using JMP® (SAS Institute Inc., Cary, NC). Pearson correlation analyses were performed to calculate the correlations of the VEP p-100 latency and amplitude with RNFL and GCIPL thickness. Spearman rho correlation analysis was used to calculate the correlations of the Pelli Robson contrast sensitivity scores with VEP p-100 latency and amplitude, RNFL and GCIPL thickness. One way analysis of variance (AVOVA) was used to compare the RNFL and GCIPL thickness between normal and delayed VEP p-100 latency status. Results were described as mean ± standard deviation. A p-value < 0.05 was considered statistically significant.

3. Results

3.1. Prevalence VEP and OCT abnormalities

Our study comprised 50 subjects (100 eyes) and their baseline demographic data are summarized in Table 1. The prevalence of VEP abnormalities was 56% while with OCT was 48% in all eyes. In patients with abnormal OCT, RNFL abnormalities were seen in 48% while GCIPL abnormalities were seen in 40% of patients. In patient with history of optic neuritis, prevalence of VEP abnormalities was 80% while in OCT it was 70% (RNFL was abnormal in 70% and GCIPL abnormal in 60%), while in patients with no prior history of optic neuritis, VEP abnormalities were seen in 40% and OCT abnormalities was seen in 33.3% of patients. (RNFL was abnormal in 30% and GCIPL was abnormal 26.%).

Table 1
Baseline Demographic data for study subjects.

Total Subjects (Number of Eyes)	50 (100)
Age in years Mean ± SD (Min-Max)	31.1 ± 7.16 (19–52)
Sex (Number of Subjects)	Males (19), Females (31)
History of Optic Neuritis (%)	20 (40%)
Disease Duration Since Diagnosis in years Mean ± SD (Min-Max)	3.94 ± 1.02 (1–5)
EDSS Mean ± SD (Min-Max)	1.23 ± 0.68 (0–3.5)

EDSS: Expanded disability status scale; SD: Standard deviation.